Using Buprenorphine for Office-Based Treatment of Opiate Addiction

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Recommendations
to the
Center for Substance Abuse Treatment (CSAT)
of the Substance Abuse & Mental Health Services Administration (SAMHSA),
from CSAT's National Advisory Council

As drafted by the Council's
Subcommittee on Buprenorphine
and as

Approved on September 15, 1999

by the full Council in open session,
after a period of public comment and discussion.

Overall Conclusions

1. The research base on buprenorphine supports the feasibility, effectiveness, and safety of providing partial agonist treatment in office-based settings. As clinical use of buprenorphine for opioid addiction treatment is introduced in the United States, additional information should be gathered and carefully assessed on its reinforcing properties in specific subpopulations, withdrawal symptomatology, and adverse effects.

2. Office-based buprenorphine treatment is desirable, since it can help to promote the shifting of opioid treatment into mainstream medicine and expand access to opioid treatment services.

3. While complying with the Controlled Substances Act (CSA), CSAT's regulations for buprenorphine treatment should follow the usual procedures and standards used in treating any medical condition and should be kept as limited and non-restrictive as possible. Any additional regulatory requirements should not be mandated in a way that identifies a patient as an addict to anyone who does not explicitly need that information for the care of the patient, or who does not have explicit consent for release of that information, as required by 42 CFR Part 2 (Vol. 42 of the Code of Federal Regulations, Part 2).

4. CSAT should work with the Drug Enforcement Administration (DEA), the Food and Drug Administration (FDA), and the States to coordinate, streamline, and hopefully to simplify the requirements that must be met by individual practitioners.

5. The new Federal regulations should allow for flexibility, provide protection against the premature "freezing" of regulatory

requirements, and allow for incorporation of new knowledge based on expanding practice experience.

6. A reasonable continuum of care should be sought for all buprenorphine patients.

7. Detailed practice guidelines should be developed and used to provide basic guidance for practitioners, including criteria for patient admission and discharge.

8. A system of practitioner selection, certification, and training will be needed to provide basic standards regarding knowledge and practice. Initially, CSAT may want to consider a system that incorporates only physicians who have demonstrable experience in addiction medicine, then later phasing in additional practitioners over time.

9. New structural models of service delivery, including links to specific pharmacies, need to be developed, tested, and then promoted with States, regions, counties, and communities.

10. New buprenorphine guidelines should allow for buprenorphine treatment practices in traditional methadone clinics, as well as in individual and group medical practices.

Specific Issues and Recommendations

1. The research base on buprenorphine supports the feasibility, effectiveness, and safety of providing partial agonist treatment in office-based settings. As clinical use of buprenorphine for opioid addiction treatment is introduced in the United States,

additional information should be gathered and carefully assessed on its reinforcing properties in specific subpopulations, withdrawal symptomatology, and adverse effects.

Assumptions

- FDA approval of the New Drug Application (NDA) for buprenorphine/naloxone (NX) will be obtained. (FDA already considers buprenorphine mono 2 and 8 mg tablets "approvable.@ The NDA for buprenorphine/NX 2 mg and 8 mg combination tablets has been filed with the FDA and is expected to be approved by December 31, 1999).

- Buprenorphine is a valuable and needed pharmacological tool for the treatment of opioid addiction with a wide margin of safety and these properties:

  - **S** Preclinical research demonstrates agonist and antagonist activities with reduced addictive potential; properties include (1) less reinforcement capacity than full agonists, (2) a ceiling effect on respiratory depression, (3) milder withdrawal symptoms from the new drug, (4) prevention of withdrawal in people with mild to moderate physical dependence on opioids, and (5) precipitation of withdrawal in moderate to severely dependent people on opioids (an antagonist effect).

  - **S** Clinical pharmacology studies show the translation of these effects to the human opioid addict population. These studies also show that the naloxone in the combination product will eliminate/attenuate the agonist effects of parenterally administered buprenorphine and will, in fact, cause severe and

acute withdrawal in anyone with even a mild physical dependence who injects the product.

- Buprenorphine fills a vital therapeutic niche in the treatment of opioid addiction in between the pure agonist effects of methadone/LAAM and the antagonist effects of naltrexone. The new product offers the following relative benefits:

  - **S** An effective medication: It works to reduce the level of heroin use and cravings.

  - **S** An extremely safe profile: It is less toxic than opioid agonists and it is nearly impossible to die from overdose, unless additional depressant drugs are being abused.

  - **S** Easier to use therapeutically: It has a slow onset and long duration of action, so it can be given once daily and, with higher doses, the dosing interval can be extended to 48 or even 72 hours.

  - **S** Easier to stop: If withdrawal occurs, it is only mild to moderate.

  - **S** Relatively low abuse potential: Naloxone will block buprenorphine effects by the intravenous (IV) but not the sublingual route, as the nalxone is not significantly absorbed when taken as directed, under the tongue.

  - **S** Good candidate for earlier stage addiction therapy: Is more likely to be appropriate for patients with initial opioid addiction characterized by a lower level of physical dependence, including young adults or adolescents.

- **S** Is effective as take-home tablets: In National Institute on Drug Abuse (NIDA) clinical trials, patients had a good response to buprenorphine combination tablets with graduated prescription allowances and with longer prescription intervals given over time.

- **S** Might be used as a transition to long-term antagonist or drug-free therapy.

Issues to be addressed

- Practice-related research is now needed on the differences in the four medications— methadone, LAAM, naltrexone and buprenorphine—particularly related to the most appropriate and promising patient profiles for each medication in terms of reducing heroin use and retaining patients in treatment.

- CSAT should aim to develop a treatment algorithm on the medications used for opioid addiction treatment. Such an algorithm will be important for precluding poor outcomes as opioid treatment extends into a wider medical treatment world.

- Information from France on deaths associated with buprenorphine should be collected, analyzed, and made available. The few deaths associated with buprenorphine have occurred with patients simultaneously using benzodiazepines and/or alcohol.

Recommendations

- At this time, Subcommittee recommendations apply only to buprenorphine as a treatment for opioid addiction.

- To improve access to buprenorphine treatment, CSAT should encourage the use of buprenorphine in risk/benefit terms. Risk/benefit analysis demonstrates that the improved availability of buprenorphine would improve access to treatment and reduce the number of preventable deaths and other adverse effects of heroin. In France, for example, the treatment of patients with buprenorphine has provided a record of both safety and public health benefits.[1]

- Although there have been a number of clinical trials, research on treatment with buprenorphine in a greater variety of settings is only now beginning. CSAT needs to stay informed of any new findings based on practice or new research and transfer this knowledge into practice guidelines in an ongoing fashion. CSAT should actively support the development of new models to deliver effective treatment for patients who do not currently have adequate access to it.

[1]The following data on the buprenorphine experience in France was received in a personal communication, August 5, 1999, from Dr. Marc Auriacombe, Laboratoire de Psychiatrie, Université Victor Segalen, Bordeaux, France: "Over a 3-year period in France (1996-98), during which a little over 50,000 patients were receiving buprenorphine at any given time, 20 so-called 'buprenorphine-related deaths' have been reported and documented. Of these, only one [involved] no associated substances (benzodiazepines and/or alcohol). All occurred among out-of-treatment subjects (black market buprenorphine). During this same time period, for 5,000 methadone subjects, 20 so-called 'methadone-related deaths' have been reported.

"During this 3-year period, overdose deaths registered by the police have gone from over 500 per year to 200 per year. The decrease is due to a decrease of heroin-related deaths; medication-related deaths are unchanged. Of course, there are many approximations in these numbers and caution is warranted, but, if anything, what is going on in France seems to support highly the incredible safety of buprenorphine considering the overall lack of control and the importance of black market access and IV diversion. ...It is clearly documented that, while buprenorphine was being delivered to opiate drug-dependent users, mortality by overdose in France decreased from 500 per year to 200 per year, which is a 60 percent decrease in 3 years." (See also Auriacombe, M.; Franques, P.; Dauloude, J.; and Tignol, J. The French experience: Results from extensive delimited research studies and nationwide sample surveys. *Research and Clinical Forums* 1999 [in press]).

2. Office-based buprenorphine treatment is desirable, since it can help to promote the shifting of opioid treatment into mainstream medicine and expand access to opioid treatment services.

Assumptions

- The United States has a huge untapped population of chronic, active opioid addicts who are not now receiving treatment. The Office of National Drug Control Policy (ONDCP) estimates that of all 810,000 American opioid addicts, a maximum of only 200,000 (fewer than 25 per cent) are now in treatment. Buprenorphine offers a tool for reaching many in this currently untapped population of at least 610,000 people with untreated or under-treated opioid problems.
- Early treatment with medication rather than simple detoxification has become increasingly critical in light of the high risk for HIV/AIDS and other infectious diseases among the drug-injecting population. Of all new HIV cases, 20,000 (50 percent) per year occur among those injecting drugs. In the United States, 95 percent of addicts who have injected drugs for 2 years or more test positive for hepatitis C, and 30 percent are positive for tuberculosis infection.

- The process used for introducing and regulating LAAM has not been very successful in expanding the number of opioid users in treatment, since only a few thousand patients nationally are being treated with LAAM. This may partly result from LAAM being caught up in the restrictions of the Federal regulations regarding methadone, with no take-home privileges being allowed since its introduction. The lessons learned from regulating LAAM need to be recognized, so similar problems can be avoided in the process of developing regulations for buprenorphine.

Issues to be addressed

- How can we design a system to ensure that HMOs include buprenorphine as a medical treatment within the medical structure? The Subcommittee is concerned that buprenorphine not be perceived as an inexpensive "magic bullet@ to be offered without the provision of other needed services.

- What measures can we take to assure physicians that they will be adequately paid for their buprenorphine patients and will not be expected to provide unreimbursed psychosocial services?

- How will we provide for patients= psychosocial needs?

- Now that we have a drug apparently useful for earlier stages of addiction, we need research to inform the value judgments that must be made. Currently, some people addicted to heroin do get better through drug-free programs. We do not know whether early opioid pharmacotherapy will decrease the possibility that young patients may eventually become drug-free. That is, if young people are put on buprenorphine "prematurely," is it possible their receptor systems will be influenced toward long-term dependency? On the other hand, could earlier effective treatment of the opioid addiction ameliorate its final outcomes? For early addicts, we must weigh their increased risk of contracting and dying from disease when treated with non-medical methods against their risk of becoming dependent on a long-term medication.

Recommendations

- In developing regulations, CSAT will need to take a long-term perspective. To greatly expand the number of patients treated in

primary care and other medical settings will require education and training about opioid treatment which is not now routinely offered or available to the medical community.

- In introducing buprenorphine treatment to the medical community, CSAT should initially address addiction medicine specialists and eventually reach out to selected primary care providers, as knowledge, experience, and training in buprenorphine treatment diffuses into general medical practice.

3. While complying with the Controlled Substances Act (CSA), CSAT's regulations for buprenorphine treatment should follow the usual procedures and standards used in treating any medical condition and should be kept as limited and non-restrictive as possible. Any additional regulatory requirement should not be mandated in a way that identifies a patient as an addict to anyone who does not explicitly need that information for the care of the patient, or who does not have explicit consent for release of that information as required by 42 CFR Part 2 (Vol. 42 of the Code of Federal Regulations, Part 2).

The Federal regulations should be made as close as possible to other medical models, which will help to destigmatize pharmacotherapy for opioid addiction treatment. The Subcommittee supported the use of *minimum* Federal regulations combined with medical credentialing standards and medical guidelines or standards of clinical practice documents.

Assumptions

- The Secretary of DHHS will probably expect the new Federal regulations to define the process for determining standards for the qualifications of practitioners and for amounts of unsupervised (take-home) medications.

- The Controlled Substances Act (CSA) and Narcotic Addict Treatment Act (NATA) will continue in force, so that unrestricted prescribing of buprenorphine by physicians is not possible. A reasonable system, consistent with existing law, will be needed to decide who should be allowed to manage and dispense buprenorphine for addiction treatment.

Issues to be addressed

- CSAT will need to set up procedures to provide a balance between the existing tensions: how to create the least restrictive regulations feasible for physicians, while also assuring quality standards that support success in treatment and prevent any catastrophes from buprenorphine treatment. It is a difficult balance to achieve at the present time, when so few physicians have had experience in treating opioid addiction with opioid agonists or antagonists and so few medical schools provide education or training in this area.

- Should urinalysis be required in the regulations as part of the usual standard of care? Subcommittee members pointed out that in private practice settings, urine testing is a routine part of treatment for such diseases as diabetes; testing does not imply a physician's lack of trust in the patient. A current NIDA opioid treatment trial is looking at how physicians make clinical decisions on the basis of urinalysis results, as well as whether physicians have been given

adequate treatment information. This ongoing research can help inform the CSAT decisions about requiring urinalysis.

Recommendations

- CSAT needs to break away from the current regulations as a framework for the new buprenorphine system. Some of the pertinent issues to look at include:

  - Consider whether we're trying to regulate physicians. Doctors treat all kinds of illness; why is addiction different? What makes these patients so different?

  - Consider whether ultimately, physicians could be deemed qualified to treat opioid addiction as they are for other diseases, by virtue of having a medical license and a recognized or peer-reviewed certification. In every area of medicine, with the exclusion only of addiction, quality assurance is a function of the State and State medical licensing boards.

4. CSAT should work with the Drug Enforcement Administration (DEA), the Food and Drug Administration (FDA), and the States to coordinate, streamline, and hopefully to simplify the requirements that must be met by individual practitioners.

The Subcommittee expressed some concern that CSAT would be creating yet another complicated system and bureaucracy for buprenorphine treatment. For example, presumably every Single State Authority (SSA) is going to have to sign off on the new system to be utilized in their State, as well as the State pharmacy boards, if the system is to utilize pharmacy dispensing (which should be recommended).

Assumptions

- Most physicians will not undertake to provide buprenorphine services unless they view this treatment in a positive light and as worth the effort expended. CSAT will need to explore and encourage positive incentives from the physician=s viewpoint, as well as to limit any disincentives related to regulation.

- The perception of oversight and paperwork can be expected to deter at least some physicians from becoming involved in buprenorphine treatment. Paperwork, licensing requirements, fees, and multiple-copy ("triplicate") forms are all psychological hurdles for physicians that need to be minimized.
- DEA will continue to cooperate in this effort; DEA is expected to require only a locked, steel cabinet for physicians who dispense limited amounts of buprenorphine in their offices rather than the level of security precautions required of treatment programs dispensing hundreds or thousands of doses. DEA will continue to require that physicians register as opioid treatment providers. DEA will exact no new security requirements for pharmacies that dispense buprenorphine.

- Because of buprenorphine's impressive margin of safety and the twin epidemics of heroin addiction and AIDS among teenagers, the Subcommittee believes that the States and other regulatory agencies are likely to be open to this approach: To keep regulations as nonrestrictive as possible and to enact standards based on scientific practice guidelines and physician judgment.

Issues to be addressed

- CSAT may wish to consider whether two levels of qualifications would be appropriate; that is, lesser requirements for physicians who will treat a limited number of buprenorphine patients. Additional qualifications might be asked of physicians who will treat a sizable number of patients, some of whom may be expected to be more complex or difficult. CSAT and DEA have already begun to explore this kind of approach by allowing physicians in the Connecticut methadone pilot project to keep small quantities of methadone in their offices under locked conditions for dispensing to a limited number of patients.

- Might it be possible for DEA to set up an addiction treatment license or registration limited to buprenorphine, accompanied by a booklet of 100 order forms and a list showing the network of participating pharmacies? Could this still be done in a manner to maintain the confidentiality of the patient from other pharmacy customers?

Recommendation

- The Subcommittee recommends that CSAT, ONDCP, and other relevant Federal agencies take a leadership role in promoting buprenorphine regulations and guidelines that will allow physicians more latitude for making clinical judgments, as with other medical conditions. Subcommittee members felt such leadership would be influential in convincing State licensing boards and other State entities to support this approach.

5. The new Federal regulations should allow for flexibility, provide protection against the premature "freezing" of

regulatory requirements, and allow for incorporation of new knowledge based on expanding practice experience.

Methadone is over-regulated in many ways, and allows little room for clinical judgment. Federal regulations both create many impediments for methadone patients and put restraints on physicians. The process of developing buprenorphine guidelines should focus on how to get past the one-paragraph barrier in the law that limits physicians in the prescribing of opioid drugs for the treatment of opiate addiction. Quality assurance of medical treatment is generally the function of State licensing boards, which usually come into play to oversee and/or restrain physicians whose care may not meet the standards of practice. However, standards of care are also important for Federal investigation regarding alleged violations of laws or regulations.

Assumptions

- Experience with methadone shows that regulations tend to become "frozen" and immutable; regulations are not law but they take on the effect of law. States have tended to use Federal regulations as a minimum or floor and then to make their own rules even more restrictive. This tendency needs to be taken into consideration in developing the buprenorphine regulations.

- Some method will be needed to assure that the new regulations can be changed to reflect growing experience and knowledge regarding practice with buprenorphine. One strategy is to place a time limit on all recommendations or on any initial pool of practitioners who have "deemed status@ as providers. Another is to enact a process into regulation that will allow modification by administrative update rather than re-regulation (for example, by means of periodically revised treatment guidelines, posted electronically).

Issues to be addressed

- Consider whether long-term Federal regulations are needed at all. After 3-5 years or so, buprenorphine may be adequately assimilated into medicine, with physicians trained and State licensing boards functioning to provide adequate quality assurance for buprenorphine treatment. At that point, Federal regulations might no longer serve any useful function except to address the discontinuity created by the Narcotic Addict Treatment Act and to give additional reassurances to the public about their safety.

Recommendation

- CSAT might consider developing a specific time limit (or "sunset") for the new Federal regulations, such as a 3-5 year limit.

6. A reasonable continuum of care should be sought for all buprenorphine patients.

The Subcommittee is concerned that physicians who treat patients with buprenorphine not be isolated from the wider addiction treatment community. The need cuts two ways: (1) each candidate for buprenorphine treatment should be assessed for a broad array of psychosocial needs, as well as heroin use and addiction, and should then be referred for help in meeting these needs; and (2) patients who do not do well on buprenorphine or who are in danger of relapse may need to be referred for assessment and therapy in a more traditional addiction treatment program. CSAT will need to consider whether this continuum of treatment can be assured through informal and individual physician arrangements, or

whether more formal and standardized agreements should be recommended.

Assumptions

- Physicians in private and group practice will not be automatically connected to the facilities needed for a continuum of care, and they may need assistance in identifying and coordinating this continuum.

Issues to be addressed

- Should buprenorphine patients be divorced from the continuum of care guidelines now being disseminated by groups such as the American Society of Addiction Medicine (ASAM), the American Psychiatric Association (APA), and soon the Veterans Administration (VA)? How will the new regulations relate to these guidelines?

- How serious is the problem of physicians who are geographically distant from any opioid treatment center? Is this common in rural areas? Is this common enough to suggest the need for some nationwide or State-by-State system (for instance, based on computer networking or telemedicine) to provide back-up support and consultation availability for individual practitioners in remote locations? Can mental health centers offer ancillary services to patients in areas without formal substance abuse treatment services?

Recommendation

- CSAT should explore the possibility of setting up regional, office-based networks for buprenorphine treatment (as well as or in conjunction with the medical maintenance networks already being created for methadone and LAAM), with physicians, treatment programs, clinics, and lists of participating pharmacies connected through the Internet.

7. Detailed practice guidelines should be developed and used to provide basic guidance for practitioners, including criteria for patient admission and discharge.

The Subcommittee recommends that practice guidelines, rather than Federal regulations, should be relied on regarding how physicians will work with different patients. Guidelines give the opportunity to attempt to inform the decision making practices of physicians. The Subcommittee, for example, prefers that guidelines and medical judgment should be used rather than regulations that specify patient eligibility according to specific frequency of use or dosage. The current Federal regulations require patients to present evidence that they have been addicted to heroin for 1 year or more before they are eligible for admission to an opioid agonist maintenance program. This would be too restrictive for buprenorphine. The Subcommittee prefers that physicians use their judgment in admitting patients to buprenorphine treatment. The decision should be based on the patient's total psychosocial picture, combined with where the patient lies along the dimensions of addiction and physical dependency.

Assumptions

- Buprenorphine will be appropriate for new types of patients not now involved in medical treatment for heroin addiction. Many patients will be young adults with shorter periods of heroin addiction and perhaps more intermittent use than current patients in traditional methadone treatment. The Subcommittee felt that if a physician sees 1 month of documented heroin addiction and an escalating pattern of abuse, then that patient should be able to enter buprenorphine treatment. This would enable patients to receive either a long enough "detox" to make a difference in outcome or short- to long-term maintenance, as indicated by clinical condition and patient response and preference, before the likelihood of becoming infected with HIV or hepatitis becomes too great. Eligible patients should include vulnerable people who are using heroin often, despite experiencing adverse effects on their lives, even if they are not physically dependent at the time of admission to buprenorphine. The Subcommittee suggested that buprenorphine may be the first pharmacotherapy of choice for many early-stage heroin addicts, particularly young opioid-dependent individuals with shorter addiction histories than the typical methadone patient. Appropriate types of patients may include:

  - People with mild to moderate physical dependence on heroin, who often snort or smoke heroin

  - People with relatively short addiction histories, such as young adults or adolescents who are at particularly high risk for serious complications of addiction, such as overdose deaths, suicide, HIV, and other infectious diseases

  - People with heroin addiction who reject the possibility of methadone maintenance treatment for themselves

- Lessons learned from NIDA's clinical trials will be used to establish the initial treatment parameters in the guidelines. Examples include:

  - Induction to buprenorphine (Trials 999A and 108A). The initial intake process was too long and cautious and patients left because of withdrawal symptoms. Patients need an effective dose of buprenorphine on the first day. Trial 108A developed an effective clinical protocol involving a 1-day intake process with 8 mg sublingual mono tablet given early on day 2, at least 6 to 8 hours after the last dose of heroin.

  - Dosing levels. At 32 mg of buprenorphine, many patients feel an increase in somatic discomfort and queasiness. They begin to experience an antagonist effect. In practice, this is a medicine with which patients often do better when the dosage is lowered rather than raised, as would generally be the case with methadone.

  - Dosing range. With flexible dosing in open label trials, about 80 percent of people tolerated doses of between 2 to16 mg per day; a few patients took doses of up to 32 mg per day before reducing their dosage. A few younger people split the dose and took buprenorphine twice a day before reducing the dosage. The highest maintenance dose of any patient in Trial 108A was 24 mg. A tablet of 2 mg or less would probably be useful to permit more gradual dose reduction.

  - Duration. Increasing the dose prolongs the duration of action and remains safe. One protocol is: 32 mg on Mondays and Wednesdays, with 48 mg on Fridays.

- Counseling. Dose adjustments should be made in conjunction with education, counseling, psychosocial support, and ongoing medical assessments and management.

Issues to be addressed

- At higher doses of buprenorphine, does a person get any more dysphoria? According to one study, it appears not. However, there is a good deal of patient variability and more research is needed on this issue.

- The practice guidelines need to define the boundaries of a "safety zone" for physicians in their treatment with buprenorphine that meets regulations and also meshes with their regular practice. Patients who would require a greater level of clinical expertise might include:

  - Patients who are abusing or are dependent on high doses of benzodiazepines or other depressants, in addition to their heroin.

  - Patients with significant psychiatric comorbidity

  - Patients who are suicidal

  - Patients who have had multiple previous treatment admissions and failures

- More experience is needed, with more data and detailed evaluation to find out about the patients' sense of wellness at different dosages; this may be individual and partly based on their past experiences.

- More experience is also needed to compare the various medications—methadone, LAAM, naltrexone and

buprenorphine**C**to tease out predictors of who might do best on which of the four medications.

Recommendations

- The "safety zone" issues should be put into best practice guidelines, not into the regulations. The "safety zone" and the physician's comfort level in making certain decisions will vary according to the physician and the situation. For example, the decision on whether to refer a patient for depression will depend on the extent of depression, whether the physician is a psychiatrist, whether a psychiatrist is available in the area, and whether the patient can afford a psychiatrist.

- Assessment of the duration of treatment relative to patient needs is an ongoing process. It should be understood that many patients will require buprenorphine for long periods of time, or perhaps even indefinitely in some cases. Premature cessation of buprenorphine therapy, as with methadone, may result in relapse. Even short periods of relapse may be dangerous in view of the attendant risks, especially infection with HIV and hepatitis C or death from acute heroin overdose. Nevertheless, buprenorphine to abstinence treatment should be available to those who want it or for whom it is clinically indicated.

- The practice guidelines should deal with how to handle the likely influx of methadone maintenance patients who hope to withdraw from methadone with buprenorphine. Although clinical trials suggest it is easier to detoxify from buprenorphine than from methadone, the likelihood of relapse after detoxification remains a danger.

- NIDA is arranging to provide CSAT with in-progress findings from its upcoming research on buprenorphine in different treatment settings; this coordination is encouraged, so that the CSAT guidelines can reflect and incorporate the most up-to-date research findings. FDA should also share pre-approval drafts of the new product labeling to facilitate the closest possible harmony between the guidelines, regulations, and the labeling.

8. A system of practitioner selection, certification, and training will be needed to provide basic standards regarding knowledge and practice. Initially, CSAT may want to consider a system that incorporates physicians who have demonstrable experience in addiction medicine, phasing in additional practitioners over time.

Although there is a well-established model for the accreditation of drug treatment facilities, there is no similar model for the accreditation of physicians. The Subcommittee recommends that the initial wave of physicians using buprenorphine be selected with some care. For instance, about 10,000 practitioners might be eligible if initial candidates were sought among those with addiction certification from the American Society of Addiction Medicine (ASAM), or board certification in addiction psychiatry or medical toxicology from the American Board of Medical Specialties (ABMS) or in addiction medicine from the American Osteopathic Association (for doctors of osteopathy [DOs]). It is important to think about the physicians' incentives for becoming credentialed and/or trained; physicians need training and a tool they can use easily. The Subcommittee discussed three different models:

a. Limiting the initial wave of eligible physicians to those with the kind of credentials listed above. In addition, these

physicians would treat buprenorphine patients only *after* completing a brief training course on the pharmacology of the new medication.

b. Allowing physicians with an interest to treat patients with buprenorphine, *provided that* they have taken a training course; this scenario would have to involve some system for selection of physicians. A model similar to this is working well in the Connecticut pilot program of medical maintenance with methadone treatment in physicians' offices. This program is having no difficulty in recruiting a variety of interested primary care physicians, who then take an 8-hour training course with continued ongoing training and clinical supervision provided. Because of the program's small size, interested physicians are selected instead of being automatically included. *The Subcommittee felt that interest and general training alone, without some credentialing or selection process (cognizant of buprenorphine), would be an insufficient standard for physicians to practice with this new treatment modality.*

c. Permitting all licensed physicians who have met State licensing requirements to offer opioid treatment with buprenorphine, perhaps with some limitation on the number of patients that any one physician would be allowed to treat with this medication, subject to specified clinical standards.

Assumptions

- Addiction-related certification will not necessarily mean that physicians are prepared to manage patients with buprenorphine. Specific training will be needed.

- Other credentialing paths with equivalence to those listed above will be needed; some physicians cannot sit for certain certification exams because they did not have the right kind of residency or they are MDs rather than DOs.

- Training will need to be brief, inexpensive, convenient, and focused to attract physicians to participate. However, these variables should not dilute appropriate training.

Issues to be addressed

- Will interested physicians, after undergoing specific training on buprenorphine, be skilled enough to treat addiction patients? What level of training will be needed to create a "safety zone" for primary care providers and others without prior addiction treatment experience or training?

- How will training be paid for? To train at least 5,000 physicians may exact a cost that Federal or State agencies may not be able or willing to pay. Alternatively, physicians in practice must believe that sufficient income can be earned to justify their own personal investments in training.

Recommendations

- Initially, training should be directed to addiction specialists.

- Appropriate certifying and other professional organizations should be encouraged to develop training courses on buprenorphine. These groups should include ASAM, the American Psychiatric Association (APA), the American Academy of Addiction Psychiatry (AAAP), the American Medical Association, the National Medical Association, the American Osteopathic Association, the American Academy of Family Physicians, the Veterans Administration (VA), and the American Methadone Treatment Association (AMTA). One prototype would be the opioid antagonist treatment (naltrexone) seminars conducted last year at several national conferences, including the American Academy of Addiction Psychiatrists.

- Physicians will need training in these areas: (1) pharmacology of the medication (dosage range, dosage variability, role of counseling in dosage, flexible dosing); (2) how-to's on assessments, including how to organize assessments and instruments for carrying out the assessment (physicians already have the skills to do assessments); and (3) providing for patients**:** other psychosocial needs.

9. New structural models of service delivery, including links to pharmacies, need to be developed, tested, and then promoted with States, regions, counties, and communities.

To meet DEA requirements as a "drug treatment program," many types of creative and non-traditional models are possible. For example, it would be possible for a county to set up a unified program, with dispersed physicians and pharmacies signing up to participate. The list of involved entities—addiction treatment clinics, physicians, and pharmacies—would constitute the "Program."

Assumptions

- A range of models will be needed, since some physicians may be willing to dispense buprenorphine through their offices, while others will want to write orders to a pharmacist. All physicians, unless it is geographically impossible, should be linked with an addiction treatment clinic or a network of clinics and providers.

Issues to be addressed

- Develop interesting ways to connect physicians to some system that will exact standards

- Explore and suggest different ways in which networks can be set up, such as through county health departments

Recommendations

- Information needs to be provided about different possible models, including:

  - The Connecticut pilot program for recovered patients on methadone, in which individual physicians get narcotic treatment program (NTP) licenses as dispensing locations from a hub methadone clinic

  - Thalidomide dispensing as a prototype model, in which physicians use a limited number of pharmacies for dispensing thalidomide to patients, with the pharmacies (or specialist pharmacists) being primarily responsible for tracking patients' medications

- The "hub" network model, being projected for CSAT=s Office-based Opioid Treatment (OBOT) program, in which a "hub" treatment clinic will connect a number of addiction treatment programs, individual practitioners, and participating pharmacies

- Practitioner/pharmacy models used in other countries, such as Australia and Canada

- On the national or State level, a standardized buprenorphine order form that could be made available to participating physicians, along with a list of pharmacies across the country that could fill the buprenorphine order. CSAT would need to ascertain from DEA whether this would be permissible or whether there would need to be specific, individual links between one physician and one pharmacy. Any special forms that may be mandated should be unrecognizable or not visible to the general public.

10. New buprenorphine guidelines should allow for buprenorphine treatment practices in traditional methadone clinics, as well as in individual and group practice.

Currently, methadone clinics have wide latitude in how they administer methadone. In some clinics, the medical decision making is really being done by program administrators, with the physicians being used to Arubber stamp@ those decisions or forced to follow dosing policies that are not consistent with well-accepted medical standards. Many physicians on staff in methadone clinics do not take adequate responsibility for dosage levels and other medical decisions. The buprenorphine regulations and guidelines

can be developed to encourage clinics toward both decision making by physicians and training in the use of buprenorphine.

Assumptions

- Buprenorphine will be administered in traditional methadone programs as well as in physician's offices.

- Training will be needed for physicians in these clinics as well as for physicians in private practice.

Issues to be addressed

- Inadequate medical decision making now occurs in some traditional methadone clinics, with non-medical clinic sponsors making or dictating medical decisions.

- There is inadequate physician interaction with patients in some clinics.

Recommendations

- Tie the management of buprenorphine to the physician's license in methadone clinics rather than to the clinic's license.

- Develop buprenorphine guidelines that are predicated on a certain level of interaction between physician and patient, which will self-select those clinics that already use physicians in this way.

- Do not automatically "grandfather" physicians in traditional methadone clinics to use buprenorphine in the absence of specific training.